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Research Article

Outcomes of Intestinal Anastomosis with or without Platelet Rich Plasma Application

Syeda Wajiha Mustafa, Malik Asad Munir, Atika Tahir, Batool Fatima*, Muhammad Azam Mirza, Muhammad Kashif Bashir

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Abstract: Background: Intestinal anastomotic leakage remains a significant clinical challenge. PRP has gained increasing attention in recent years due to its potential therapeutic benefits in various medical applications.

Objective: To evaluate the effect of PRP application on outcomes of intestinal anastomosis among pediatric patients in a tertiary care hospital.

Materials and Methods: This prospective cohort study was performed at Department of Pediatric Surgery, Mayo Hospital, Lahore, Pakistan, during 1st December 2024 to 30th September 2025, after obtaining ethical approval bearing number 841/RC/KEMU. After through assessment of underlying pathology intraoperatively, the surgeon decided either for conventional approach or PRP. Group P received PRP was administered between the two layers of the anastomosis whole Group C did not receive PRP application.

Result: A total of 160 patients were studied with equal allocation in both of the cohorts (i.e. 80 in each cohort). Anastomosis time was significantly higher in Group P than Group C (35 versus 30, p<0.001). Anastomosis leakage (5% versus 15%, p=0.261) and adhesion related obstruction (7.5% versus 15%, p=0.480), duration of nasogastric tube (4.7±1.1 versus 5.2±1.9, p=0.090), length of hospital stay (13.1±3.4 versus 14.5±2.7, p=0.070) were lower in Group P than Group C but it did not reach statistical significance.

Conclusion: The findings of the present study suggested a consistent trend towards better outcomes in the PRP group than control group in terms of anastomosis specific outcomes including anastomotic leakage and adhesions related obstruction and recovery parameters including shorter duration of nasogastric tube and length of hospital stay. The findings should be verified in a large scale, multicenter study for establishing the superiority of PRP than conventional approach.

Keywords: Anastomosis leakage, Intestinal anastomosis, Platelet-rich plasma therapy, Pediatric surgery, Hyperthermia, Inflammatory disease.

INTRODUCTION

Intestinal anastomosis is one of the most often performed surgical procedures in the fields of general and gastrointestinal surgery. Furthermore, one common surgical technique in pediatric surgery is elective intestinal anastomosis. This method is utilized to treat inflammatory diseases, functional or anatomic congenital malformations, and intestinal continuity (ileostomy or colostomy closure) [1]. Patients of many ages, ailments, and etiologies have the surgery, including those with Crohn's disease or malignant lymphoma in teens and necrotizing enterocolitis or duodenal atresia in newborns [2]. Severe consequences, including sepsis, peritonitis, or death from complications after gastrointestinal resection surgery, can result from improperly executed anastomoses [3].

Complications from bowel anastomosis are common in individuals having extensive abdominal surgery that involves bowel resection. With rising morbidity and mortality, gastrointestinal anastomotic leaks remain the surgeon's worst nightmare among all complications, resulting in longer hospital stays and higher hospital expenses. Intestinal leaks still occur in 5–10% of cases worldwide, despite advancements in technology and the manufacturing of sophisticated instruments (such as robotic and laparoscopic surgery) [4, 5].

Two categories of causes including local and systemic factors are investigated for intestinal anastomotic leaks. Local factors include surgical technique and suture materials, tension and inadequate blood flow in anastomosis, presence of healthy tissue tips, bacterial contamination, distal obstruction, hyperthermia, radiation damage, mechanical trauma, and antibiotic use; systemic factors include hypoalbuminemia, hypovolemia, severe anemia, acidosis, sepsis, immunosuppression, diabetes mellitus, malignancy, and cachexia due to malnutrition [6, 7].

Local applications are a significant component linked to anastomotic strength. Despite the fact that a variety of materials have been employed to increase anastomosis potency, no perfect treatment has yet been identified. In this regard, regenerative medi-

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cine might provide some crucial direction [8]. Platelets release growth factors, which are polypeptide molecules with various structures and roles. The most important ones are platelet-driven growth factor (PDGF), insulin-like growth factor (IGF), vascular endothelial growth factor, fibroblast growth factor (FGF), and transforming growth factor (TGF-b). These elements are known for their chemotactic and mitogenic properties, which facilitate to the healing of wounds [9, 10].

The use of platelet-rich plasma (PRP) is a recently proposed technique. Marx was the first to suggest this word in 1998 [11]. Platelet-rich plasma guarantees that platelets penetrate in excess, hastening the healing of wounds. Modulating growth factors including insulin-like growth factor, platelet-derived growth factor, and transforming growth factors β1 and β2 can explain the regeneration impact [12, 13]. Within ten minutes of coagulation, the blood coagulation process triggers the active release of these components. The first hour is when almost 95% of growth factors are produced [14].

Despite improvements in surgical methods, intestinal anastomotic leakage continues to be a major clinical problem that increases morbidity, lengthens hospital stays, and increases death. PRP's potential therapeutic effects in a range of medicinal applications have drawn more attention in recent years [15]. The clinical results in the literature now in publication vary, and further research is required to fully understand the molecular processes by which PRP affects the intestinal tissues' healing cascade. Therefore, the purpose of this study is to thoroughly assess how PRP affects intestinal anastomosis healing, with an emphasis on how it can alter important growth factors and enhance clinical results for young patients in a tertiary care facility.

MATERIALS AND METHODS

This prospective cohort study was performed at Pediatric Surgery Department, of Mayo Hospital in Lahore, Pakistan, during 1st December 2024 to 30th September 2025. The study received a formal ethical approval bearing number 841/RC/KEMU. Patients of age 1-13 years of either gender planned to undergo elective intestinal were included. Patients having shock, malnourished, diabetes, hypoalbuminemia, anemia, malignancy and undergoing revision surgery were excluded.

Since no such study was existing on pediatric population, so a pilot study was performed taking 30 patients in each arm. In pilot results, none of the patients had anastomosis leakage in PRP group while 10% patient developed it. Using an approach of two proportion sample size calculation via WHO sample size calculator at power of 80% and 95% confidence interval, a sample of 74 patients per arm was estimated. Patients were enrolled into the study in a consecutive manner with written permission of their parents either mother or father or Guardian.

All the patients planned to undergo the elective procedure were admitted a day before surgery to assess their medical fitness. Based on the hospital protocol, their laboratory and imaging investigation were done. As per the schedule patients were moved to the operation theater. The procedure was performed by a consultant surgeon having at least 5 years of relevant experience. Exploratory laparotomy was carried out under general anesthesia. The underlying pathophysiology was determined and a two layered intestinal anastomosis was carried out with vicryl 3/0 as per the pre-defined surgical technique. On intra-operative assessment of underlying pathology the surgeon took a decision either for conventional approach or PRP.

Platelet-Rich Plasma (PRP) was prepared by a standard two-step determination following the collection of approximately 9.5 ml of blood via venipuncture under aseptic conditions and then placed in PRP tubes containing 0.5 ml of buffered sodium citrate. The first centrifugation was performed at 200 g for 10 minutes at 22°C, and the supernatant plasma was transferred in a new sterile centrifuge tube to be centrifuged again at 400 g, at 22°C, to obtain approximately 1 ml of PRP. All PRP preparations were completed before the surgical procedure to optimize efficiency. Group P received PRP was administered between the two layers of the anastomosis whole Group C did not receive PRP application. Both groups received identical broad-spectrum antibiotic therapy postoperatively. Patients were maintained on NPO status until the return of bowel sounds and cessation of nasogastric tube output. Mobilization was initiated upon full recovery of consciousness.

Patients were discharged on when they showed no complications and exhibited restored bowel continuity, as evidenced by audible bowel sounds, acceptance of oral intake, and normal flatus and stool passage. The occurrence of anastomotic leakage was monitored till their discharge. Cases of leakage underwent re-do laparotomy and stoma creation. Any additional complications were managed in accordance with the established ward protocols.

Anastomosis time was the time interval between placements of first stich of anastomosis to the last cut of the final suture at completion. Anastomotic leakage was identified during clinical assessment by the treating consultant. The presence of abdominal pain, fever, and/or vomiting, along with a tense and tender abdomen upon palpation and the observation of gas beneath the right dome of the diaphragm on chest radiographs consistent with clinical manifestations, constituted the criteria for diagnosing leakage. Adhesion relation obstruction was confirmed based on clinical signs including vomiting, abdominal distension, flatus or failure to pass stool with radiological findings indicating small bowel obstruction either on abdominal X-ray or contrast-enhanced CT. Features such as dilated small bowel loops with multiple air-fluid levels and a transition point with evidence of a mass were considered as suggestive of small bowel obstruction.

STATISTICAL ANALYSIS

Data was entered and analyzed using SPSS version 27. Categorical variables were summarizes as frequency and percentage.

Numerical variables were presented mean ± standard deviation after confirming normal distribution with Shapiro-Wilk test. Pearson Chi-square test or Fisher-exact test was applied to compare categorical variables among two study groups whereas numerical parameters were compared using Independent t-test. P-value less than or equal to 0.05 was considered as statistically significant.

RESULT

A total of 160 patients were studied with equal allocation in both of the cohorts (i.e. 80 in each cohort). Intraoperative visualization demonstrating intestinal anastomosis with and without PRP is depicted in Fig. (**1**).

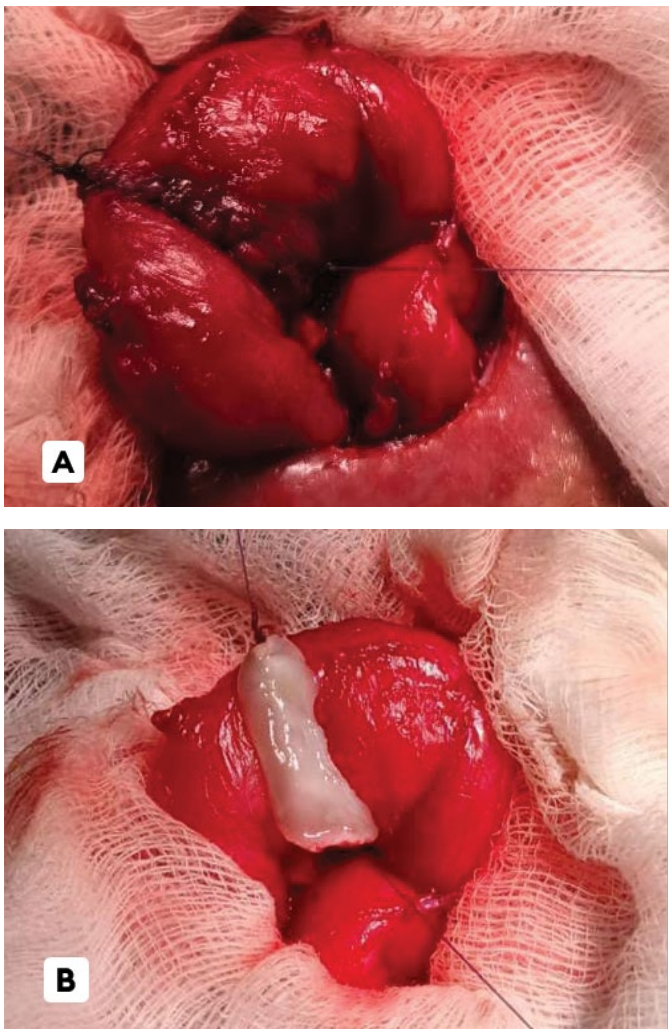

Fig. (1). (**A**): Displays Ileoileal Anastomosis without PRP Application; (**B**): Shows Application of PRP on Sture Line.

Table **1** displays comparison of patients' sociodemographic, surgery related and preoperative laboratory investigations. None of the feature was significant different among Group P and Group C except mild adhesion (p=0.006).

Table 1. Comparison of Patients' Features among the Two Study Cohorts.

Variables	Group P	Group C	p-value
Sociodemographic Features			
Age, n(%)			
1-5 years	43(53.7)	31(38.7)	0.081
6-13 years	37(46.3)	49(61.3)	
Gender, n(%)			
Male	40(50)	41(51.3)	0.825
Female	40(50)	39(48.7)	
BMI for age z-score, mean ± SD	0.47±0.05	0.42±0.08	
Surgery Related Parameters, n(%)			
Surgery Indication			
Intestinal atresia	37(46.3)	35(43.7)	0.887
Ileostomy closure	25(31.3)	24(30)	
Intussusception	18(22.5)	21(26.3)	
Type of Anastomosis, n(%)			
Ileoileal	29(36.3)	25(31.3)	0.364
Ileocolic	39(48.7)	35(43.7)	
Colocolic	12(15)	20(25)	
Intraoperative Findings, n(%)			
Mild adhesion	57(71.3)	39(48.7)	*0.006
Dense adhesion	7(8.7)	15(18.7)	0.108
Colon anastomosis	43(53.7)	41(51.3)	0.874
Small intestine anastomosis	13(16.3)	19(23.7)	0.323
Ileocolic anastomosis	24(30)	21(26.3)	0.725
Preoperative Laboratory Parameters			
Hemoglobin (g/dL), mean ± SD	12.1±3.2	11.9±2.8	0.971
White blood cells, mean ± SD	8.6±2.7	8.8±2.8	0.896
C-reactive protein (mg/L), mean ± SD	6.1±1.7	6.3±1.4	0.925
Serum albumin (g/dL), mean ± SD	3.9±0.09	4.2±0.1	0.714

*Significant at p<0.05.

Table **2** compares anastomosis specific outcomes and recovery outcomes among Group P and Group C. anastomosis time was significantly higher in PRP group than control group (p<0.001). Time of first bowel movement was lower in PRP group than control group (p=0.006). Anastomosis leakage (p=0.261), adhesion related obstruction (p=0.480), duration of nasogastric tube (p=0.090), length of hospital stay (p=0.074) and mortality rate (p=0.492) were not significantly different among the two study groups.

Table 2. Comparison of Anastomosis Specific Outcomes and Recovery Outcomes among Group P and Group C.

Variables	Group P	Group C	p-value
Anastomosis specific outcomes			
Anastomosis time in minutes, mean ± SD	35±11.2	30±15.8	*<0.001
Anastomotic leakage, n(%)	4(5)	12(15)	0.261
Adhesion related obstruction, n(%)	6(7.5)	12(15)	0.480
Recovery outcomes			
Time of first bowel movement, mean ± SD	2.2±0.5	2.6±0.8	*0.006
duration of nasogastric tube, mean ± SD	4.7±1.1	5.2±1.9	0.090
length of hospital stay, mean ± SD	13.1±3.4	14.5±2.7	0.074
Mortality, n(%)	0(0)	4(5)	0.492

*Significant at p<0.05.

DISCUSSION

Intestinal anastomosis in the pediatric population is among the most technically challenging and highest-risk pediatric surgical procedures. Healing at the site of the anastomosis relies on several variables such as tissue perfusion, bowel wall integrity, and contamination. The administration of platelet-rich plasma (PRP) is suggested to improve anastomotic healing as it releases growth factors that promote angiogenesis, fibroblast proliferation, and collagen synthesis. In this study, the decision to apply PRP whenever applicable was made by the operating surgeon based upon their intraoperative evaluation of tissue vascularity, fullness of bowel wall thickness, degree of contamination, patient stability, and PRP preparation. Due to these clinical variables, and the well-being of the patients, randomization was not possible or feasible in an ethical manner. Therefore, a cohort study design was chosen to depict real-life surgical decision-making in a pediatric high-risk population.

Our study demonstrated a significantly longer mean anastomosis time in the PRP group, as compared to the non-PRP group (35 min vs 30 min, $p < 0.001$). This prolonged duration is more likely attributed to the extra step to prepare and apply PRP, and, not to a technical difficulty with the anastomosis itself. The duration to mix, activate and apply PRP, accounts for several minutes in total operative time, and thus, to the statistically significant difference. The literature on adult humans shows no comparable findings, as most prior work only studies postoperative outcomes, and not necessarily duration of procedure. The clinical reports by Shamiyeh *et al.* [16] and Valsamidis *et al.* [17] using the Obsidian®ASG, an autologous platelet-rich fibrin matrix, demonstrated proof of concept for technical feasibility and safety of PRP application within colorectal anastomosis, though did not measure time of operation. Animal models provided similar findings from a procedural standpoint. A systematic review of experimental models demonstrated that PRP application typically added around 5 to 10 minutes of time on to operative time because of the time required for preparation, but improved the quality of the anastomosis in every experimental model, with bursting pressure improved by 30 to 40 percent compared to the control [18]. Therefore, the increased time reported in our series seems like a fair trade for the biologic use of PRP because of its reported biologic effects such as increased vascularity, collagen maturation, and increase in anastomotic valve. Note that this is a strength which transformed this study's reported time outcome from being statistically insignificant to being clinically significant, but without being clinically relevant.

Leakage of anastomotic site is a major problem following intestinal anastomosis. In our series, PRP group had a lower rate of leakage (5%) than non-PRP group (15%), but this was not statistically significant ($p=0.261$). However, the 10% absolute reduction is clinically significant, particularly in pediatric patients, as a single leak can result in considerable morbidity. In a randomized controlled trial by Sbh and Al-Shalabi [19], involving adults undergoing colorectal anastomosis, the leak rate dropped from 13.3% to 0% with PRP injection, demonstrating an important statistically significant benefit. In a similar vein, Shamiyeh and colleagues [16] reported a prospective clinical series of rectal resections using an autologous platelet-rich fibrin matrix, Obsidian®ASG, having only 1 leak among 35 patients, while Valsamidis and colleagues [17] found no major leak in their series of 20 patients, further supporting the potential for platelet-based therapy to improve the healing of surgical anastomoses. These protective effects are most likely mediated by improved fibrin scaffold formation, localized growth factor delivery, and accelerated healing of tissues under the wound with cellular regeneration. The lower leak rate in our pediatric series directionally aligns with these adult studies and are also supported by animal studies that have reported an increase in bursting pressure, improved collagen deposition and improved histological healing, following treatment with PRP [18, 20, 21]. Overall, these data suggest a potential for PRP to provide a clinically meaningful protective effect on anastomotic integrity among pediatric patients, particularly in high-risk children, even if we failed to attain statistical significance in our small sample.

The incidence of adhesion-related obstruction was also lower in the PRP cohort (7.5% vs 15%, $p = 0.48$). While this potential difference fell short of significance, it was consistent with animal studies. In a study with 24 Wistar albino rats, [4] administer cecal incision and repair (suture) along with an intraperitoneal infu-

sion of PRP (3 mL) or saline. The PRP cohort exhibited lower infiltration scores of neutrophil, lymphocyte/plasmocyte, and histiocyte infiltration across inflammatory markers, along with attenuated fibrosis at day 7 ($p < 0.05$). In another animal study, PRP gel exhibited lower adhesion area and strength compared to hyaluronic acid in a rat model (mean scores for adhesion = PRP group ≈3.2 ± 1.5 vs control 8.1 ± 1.7, $p < 0.001$) [22]. These studies support the hypothesis that PRP may reduce the incidence of postoperative adhesion due to it occurring through modulation of fibroblast activity and inflammation with the peritoneum. However, in clinical situations, even a modest reduction in obstruction related to postoperative adhesion is important, since postoperative adhesive disease is a significant reason for re-operation in pediatric surgery.

In summary, while the observed reductions in both adhesions and leakage may not be statistically significant, they are suggestive of important clinical benefit, and are thus consistent with the biological rationale and preclinical evidence for the use of PRP. The PRP might be superior to the control condition since an activated, concentrated source of growth factors and cytokines is delivered to the site of injury, acting to modulate fibroblast activity, promote organized collagen deposition, and lower peritoneal inflammation - all of which are properties that mitigate adhesion formation. The lack of statistical significance for our pediatric sample cohort could be attributed to small sample sizes and low absolute event rates coupled with interpatient variability in healing response behavior that limited the power to detect differences, but the directional trend appears to hold clinical significance given that even modest reductions in adhesion can lessen reoperation risk and improve postoperative outcomes. Nonetheless, large adequately powered pediatric studies are necessary to confirm these findings.

In terms of recovery parameters, time to first bowel movement was statistically significantly shorter in the PRP (2.2 ± 0.5 days) than the non PRP group (2.6 ± 0.8 days; $p = 0.006$). This is statistically significant, and is of clinical importance, as it reflects the earliest return and restoration of bowel motility and less postoperative ileus. While there are human based studies using platelet rich matrices (i.e. Obsidian® ASG) that examine data on anastomotic leak rates, and feasibility studies, no studies reported time to first bowel movement or any recovery time variables [16,17]. As such, our data is novel for the pediatric population and additionally aligns with animal studies, showing that PRP improves local perfusion, collagen maturation and healing of the suture line and promotes an earlier return of gastrointestinal motility [18, 20].

The PRP group had a shorter duration of nasogastric tube placement (4.7 ± 1.1 versus 5.2 ± 1.9; $p = 0.09$) and length of stay (13.1 ± 3.4 versus 14.5 ± 2.7; $p = 0.07$).While not statistically significant, these results reflect a favorable trend towards faster recovery for PRP treated patients. Most of the human based studies reported anastomotic leak rates, feasibility and safety. No data was published around nasogastric tube duration or length of stay [1-3]. Clinically, even a 1-1.5 day decreased length of stay can be meaningful for decreasing health care costs and patient comfort, especially in children.

In our study, mortality was seen only in the non-PRP group (5 %, $p = 0.492$). While the sample size precludes any definitive conclusions, the lack of fatalities in the PRP group suggests that intraoperative PRP use is safe. None of the human studies considered have presented adverse events associated with the use of PRP [16, 17, 19], and the animal studies also indicate that PRP has a good safety profile [18, 20, 21, 23-25]. PRP therefore appears to be a safe adjunct for pediatric intestinal anastomosis.

STRENGTH

The primary strength of this study is the pediatric patient population (age 1 to 13), which is limited in literature discussing PRP. The majority of the human literature pertains to adult colorectal procedures; therefore, our study adds new evidence for children undergoing different types of intestinal anastomoses. The pragmatic cohort design allowed surgeons' decisions to reflect clinical judgment in real world practice, which further enhances external validity. This study also assessed both anastomosis specific and recovery outcomes for an all-in-one assessment of PRP in the perioperative setting.

LIMITATIONS

This investigation has numerous limitations. Firstly, the surgeon-directed allocation of PRP may have introduced potential selection bias, as PRP may have been preferentially applied to patients with better intraoperative conditions. In addition, being a single-center study may limit generalizability, and did not assess long-term outcomes like late adhesive obstruction. Finally, any comparison to adult studies or animal models should be taken with caution, as there are significant physiological and anatomical differences between children and adults.

CONCLUSION

The findings of the present study suggested a consistent trend towards better outcomes in the PRP group than control group in terms of anastomosis specific outcomes including anastomotic leakage and adhesions related obstruction and recovery parameters including shorter duration of nasogastric tube and length of hospital stay. The findings should be verified in a large scale, multicenter study for establishing the superiority of PRP than conventional approach.

ABBREVIATIONS

FGF: Fibroblast Growth Factor.

IGF: Insulin-Like Growth Factor.

PDGF: Platelet-Driven Growth Factor.

PRP: Platelet-Rich Plasma.

TGF-β: Transforming Growth Factor.

AUTHORS' CONTRIBUTION

Syeda Wajiha Mustafa: Conceptualization, Methodology, Data analysis and interpretation, Writing draft, Final approval, final proof to be published.

Malik Asad Munir: Conceptualization, Study design, Critical review and revision the manuscript, Final approval, final proof to be published.

Atika Tahir: Study design, Methodology, Data analysis and interpretation, Writing draft, Final approval, final proof to be published.

Batool Fatima: Conceptualization, Methodology, Data analysis and interpretation, Critical review and revision the manuscript, Final approval, final proof to be published.

Muhammad Azam Mirza: Methodology, Data analysis and interpretation, Writing draft, Final approval, final proof to be published.

Muhammad Kashif Bashir: Conceptualization, Final approval, final proof to be published.

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Declared none.

ETHICAL DECLARATIONS

Data Availability Statement

All of the data collected for this study is presented in results.

Ethical Approval

The study received a formal ethical approval bearing number 841/RC/KEMU.

Consent to Participate

A written informed consent was sought from either parents or care taker of the children as appropriate.

Consent for Publication

All authors take responsibility of the integrity of the work and give consent for publication.

Conflict of Interest

Declared none.

Competing Interest / Funding

Declared none.

Use of AI-Assisted Technologies

The authors declare that no generative artificial intelligence (AI) or AI-assisted technologies were utilized in the writing of this manuscript, in the creation of images/graphics/tables/captions, or in any other aspect of its preparation.

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